General

Guideline Title

Diabetes technology—continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: an Endocrine Society clinical practice guideline.

Bibliographic Source(s)

Peters AL, Ahmann AJ, Battelino T, Evert A, Hirsch IB, Murad MH, Winter WE, Wolpert H. Diabetes technology-continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2016 Nov;101(11):3922-37. [119 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Klonoff DC, Buckingham B, Christiansen JS, Montori VM, Tamborlane WV, Vigersky RA, Wolpert H, Endocrine Society. Continuous glucose monitoring: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011 Oct;96(10):2968-79.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the quality of the evidence (+OOO, ++OO, +++O, and ++++); the strength of the recommendation (1 or 2); the difference between a "recommendation" and a "suggestion," and the definition of "best practice statements" are provided at the end of the "Major Recommendations" field.

Insulin Pump Therapy without Sensor Augmentation

The Task Force recommends continuous subcutaneous insulin infusion (CSII) over analog-based basal-bolus multiple daily injections (MDI) in patients with type 1 diabetes mellitus (T1DM) who have not achieved their A1C goal, as long as the patient and caregivers are willing and able to use the device. (1|+++O)

The Task Force recommends CSII over analog-based basal-bolus MDI in patients with T1DM who have achieved their A1C goal but continue to experience severe hypoglycemia or high glucose variability, as long as the patient and caregivers are willing and able to use the device. (1|++OO)

The Task Force suggests CSII in patients with T1DM who require increased insulin delivery flexibility or improved satisfaction and are capable of using the device. (2|++OO)

Insulin Pump Therapy in Type 2 Diabetes Mellitus

The Task Force suggests CSII with good adherence to monitoring and dosing in patients with type 2 diabetes mellitus (T2DM) who have poor glycemic control despite intensive insulin therapy, oral agents, other injectable therapy, and lifestyle modifications. (2|++OO)

Insulin Pump Use in the Hospital

The Task Force suggests that clinicians continue CSII in patients admitted to the hospital with either type of diabetes if the institution has clear protocols for evaluating patients as suitable candidates and appropriate monitoring and safety procedures. (2|++OO)

Selection of Candidates for Insulin Pump Therapy

The Task Force recommends that before prescribing CSII, clinicians perform a structured assessment of a patient's mental and psychological status, prior adherence with diabetes self-care measures, willingness and interest in trying the device, and availability for the required follow-up visits. (1|++OO)

Use of Bolus Calculators in Insulin Pump Therapy

The Task Force suggests encouraging patients to use appropriately adjusted embedded bolus calculators in CSII and have appropriate education regarding their use and limitations. (2|++OO)

Real-Time Continuous Glucose Monitors in Adult Outpatients

The Task Force recommends real-time continuous glucose monitoring (RT-CGM) devices for adult patients with T1DM who have A1C levels above target and who are willing and able to use these devices on a nearly daily basis. (1|++++)

The Task Force recommends RT-CGM devices for adult patients with well-controlled T1DM who are willing and able to use these devices on a nearly daily basis. (1|++++)

Use of Continuous Glucose Monitoring in Adults with Type 2 Diabetes Mellitus

The Task Force suggests short-term, intermittent RT-CGM use in adult patients with type 2 diabetes mellitus (T2DM) (not on prandial insulin) who have A1C levels ≥7% and are willing and able to use the device. (2|++OO)

Education and Training on the Use of Continuous Subcutaneous Insulin Infusion and Continuous Glucose Monitoring

The Task Force suggests that adults with T1DM and T2DM who use CSII and continuous glucose monitoring (CGM) receive education, training, and ongoing support to help achieve and maintain individualized glycemic goals. (Ungraded Good Practice Statement)

Definitions

Quality of the Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

Ungraded Good Practice Statement: In this guideline, the Task Force made several statements to emphasize the importance of shared decision making, general preventive care measures, and basic principles of diabetes technology. They labeled these "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised and was considered out of the scope of this guideline. The intention of these statements is to draw attention and remind providers of these principles; one should not consider these statements as graded recommendations.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Type 1 diabetes mellitus (T1DM)
- Type 2 diabetes mellitus (T2DM)

Guideline Category

Management

Technology Assessment

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To assess all available data on existing and emerging technologies and procedures for improving glucose control for patients with diabetes
- To formulate clinical practice guidelines for the use of continuous glucose monitoring and continuous subcutaneous insulin infusion in adults with diabetes

Target Population

Adults with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM)

Interventions and Practices Considered

1. Continuous subcutaneous insulin infusion (CSII) (versus analog-based basal-bolus multiple daily injections [MDI]) in type 1 (T1DM) and type 2 diabetes mellitus (T2DM) patients
2. CSII in hospitalized patients

3. Selection of candidates for CSII
4. Use of appropriately adjusted embedded bolus calculators in CSII
5. Use of real-time continuous glucose monitoring (RT-CGM) devices in T1DM and T2DM patients
6. Patient education, training, and ongoing support in CSII and RT-CGM

Major Outcomes Considered

- Hemoglobin A1c (HbA1c) (baseline, during follow up, at the endpoint)
- Number of events of hypoglycemia (whether symptomatic or not, value of glucose)
- Time spent in hypoglycemia

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse: The Task Force commissioned a systematic review and individual patient data meta-analysis of randomized controlled trials (RCTs) (see the "Availability of Companion Documents" field) and also used the best available evidence from other published systematic reviews and individual studies.

Methods

The reviewers included randomized trials (RCTs) that enrolled patients with diabetes mellitus type 1 and compared real-time continuous glucose monitoring (RTCGM) versus control group (usually a blinded RTCGM) and reported the outcome of interest (hemoglobin A1c [HbA1c] at baseline and follow up, time spent in hypoglycemia, and number of hypoglycemic events).

Several databases were searched from each database's earliest inception until January 2015, without language restrictions (Ovid Medline In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus). Controlled vocabulary supplemented with keywords was used.

Abstracts and titles that resulted from executing the search strategy were independently evaluated by two reviewers for potential eligibility and the full text versions of all potentially eligible studies were obtained. Two reviewers working independently considered the full text reports for eligibility. Disagreements were reconciled by consensus and if not possible by consensus through arbitration by a third reviewer.

Number of Source Documents

The initial search resulted in 760 citations, and after abstract screening reviewers identified 134 potentially relevant studies. After full text screening, reviewers finally included 11 studies (1530 patients).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of the Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

Methods Used to Analyze the Evidence

Meta-Analysis of Individual Patient Data

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse: The Task Force commissioned a systematic review and individual patient data meta-analysis of randomized controlled trials (RCTs) (see the "Availability of Companion Documents" field) and also used the best available evidence from other published systematic reviews and individual studies.

Methods

A list of potential included studies was sent to the Endocrine Society Task Force developing the guideline on real-time continuous glucose monitoring (RTCGM) for verification. The corresponding author of each trial was contacted via emails requesting individual patient data. Data from each participant included (when available): demographics (age, sex, ethnicity), hemoglobin A1c (HbA1c) (baseline, during follow-up, at the endpoint), follow-up period, number of events of hypoglycemia (whether symptomatic or not, value of glucose), time spend in hypoglycemia, time of the episode of hypoglycemia (night, day, after exercise/playtime for children), type of device/manufacture/sensor versus no sensor, body mass index (BMI), weight, skill level and education provided to patient/parents' education, adherence to wearing the device, diabetes duration, and insulin delivery system (pump versus multiple daily injections). The reviewers used the Cochrane risk of bias tool to appraise the methodological limitations of each trial.

Data were analyzed using Stata Statistical Software: Release 14 (College Station, TX: StataCorp LP). A two-step regression model was used to estimate the pooled difference in means for HbA1c and time in hypoglycemia with 95% confidence intervals (CI). When reported, the reviewers pooled the mean number of hypoglycemic events in each arm. Subgroup analysis was based on age and sex.

Risk of Bias Assessment

The overall risk of bias in the included trials was moderate to high. Quality was downgraded mainly due to not reporting allocation concealment, lack of outcome assessor blinding and source of funding (in all trials, funding source was for profit companies).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Participants

The participants include an Endocrine Society-appointed Task Force of seven experts, a methodologist, and a medical writer. The American Association for Clinical Chemistry, the American Association of Diabetes Educators, and the European Society of Endocrinology co-sponsored this guideline.

Evidence

The Task Force developed this evidence-based guideline using the Grading of Recommendations Assessment, Development and Evaluation system to describe the strength of recommendations and the quality of evidence. The Task Force commissioned one systematic review and used

the best available evidence from other published systematic reviews and individual studies.

Consensus Process

One group meeting, several conference calls, and e-mail communications enabled consensus.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

1- Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

Ungraded Good Practice Statement: In this guideline, the Task Force made several statements to emphasize the importance of shared decision making, general preventive care measures, and basic principles of diabetes technology. They labeled these "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised and was considered out of the scope of this guideline. The intention of these statements is to draw attention and remind providers of these principles; one should not consider these statements as graded recommendations.

Cost Analysis

A cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Committees and members of the Endocrine Society, the American Association for Clinical Chemistry, the American Association of Diabetes Educators, and the European Society of Endocrinology reviewed and commented on preliminary drafts of these guidelines.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The goal of glucose management in all types of diabetes is to minimize and hopefully eliminate the acute and chronic complications associated with diabetes, such as the risks of microvascular complications and potentially (to a lesser degree) macrovascular complications and mortality. All persons with type 1 diabetes mellitus (T1DM) require insulin, and persons with type 2 diabetes mellitus (T2DM) frequently need insulin for adequate glucose control. Advances in the pharmacokinetics and pharmacodynamics of insulin products and in the methods of insulin delivery and glucose monitoring are geared toward improving glucose control, minimizing hypoglycemia, and improving quality of life. Two such advances include continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM).

- Despite the limitations of the available literature, there is relatively consistent evidence that current CSII is likely to improve glucose control in motivated patients with inadequate glucose control who are appropriately educated and supported.

Refer to the evidence sections in the original guideline document for additional discussion of the balance of benefits versus harms of CSII and CGM.

Potential Harms

Intensification of insulin therapy increases the risk of hypoglycemia, which is associated with both morbidity and mortality.

Refer to the evidence sections in the original guideline document for additional discussion of the balance of benefits versus harms of continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM).

Qualifying Statements

Qualifying Statements

- The Endocrine Society's clinical practice guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgement of healthcare providers and each patient's individual circumstances.
- The Endocrine Society makes no warranty, express or implied, regarding the guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect, special, incidental, or consequential damages related to the use of the information contained herein.

Implementation of the Guideline

Description of Implementation Strategy

See the following tables in the original guideline for outlines on suggested education and training for continuous subcutaneous insulin infusion (CSII) and real-time continuous glucose monitoring (RT-CGM):

- Table 1. CSII—Considerations for Education and Training
- Table 2. RT-CGM Technology—Considerations for Education and Training for Personal Use
- Table 3. Suggested Health Care Provider Resources to Support the Safe and Effective Use of CSII and RT-CGM

Implementation Tools

Mobile Device Resources

Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Peters AL, Ahmann AJ, Battelino T, Evert A, Hirsch IB, Murad MH, Winter WE, Wolpert H. Diabetes technology-continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2016 Nov;101(11):3922-37. [119 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Nov

Guideline Developer(s)

The Endocrine Society - Professional Association

Source(s) of Funding

The Endocrine Society provided all funding for this guideline; the Task Force received no funding or remuneration from commercial or other entities.

Guideline Committee

Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring Task Force

Composition of Group That Authored the Guideline

Task Force Members: Anne L. Peters (*chair*), Andrew J. Ahmann, Tadej Battelino, Alison Evert, Irl B. Hirsch, M. Hassan Murad, William E. Winter, Howard Wolpert

Financial Disclosures/Conflicts of Interest

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All Task Force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The Clinical Guidelines Subcommittee (CGS) reviews all conflicts of interest before the Society's Council approves the members to participate on the Task Force and periodically during the development of the guideline. All others participating in the guideline's development must also disclose any conflicts of interest in the matter under study, and a majority of these participants must be without any conflicts of interest. The CGS and the Task Force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests (e.g., stocks and stock options [excluding diversified mutual funds]); honoraria and other payments for participation in speakers' bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

Financial Disclosures of the Task Force*

Anne L. Peters, MD (chair)—Financial or Business/Organizational Interests: Medscape-Education (Advisory Board), ABIM-Board Examinations (Endocrine Subspecialty Board), American Diabetes Association (Speaker), USFDA (Consultant), Lexicon (Advisory Board), NIH (Grantee to Institution), Helmsley Charitable Trust (Grantee to Institution), JDRF (Committee Member), Bigfoot Biomedical (Advisory Board), OptumRx (Ad Hoc Consultant), CVS/Caremark (Ad Hoc Consultant), Omada Health (Advisory Board); Significant Financial Interest or Leadership Position: Abbott Diabetes Care (Advisory Board), Astra Zeneca (Advisory Board), Biodel (Advisory Board), Lilly (Advisory Board/Speaker), Becton Dickinson (Advisory Board), Merck (Advisory Board), Janssen (Advisory Board/Speaker/Principal Investigator [Grantee]), Medtronic (Principal Investigator [Grantee]), Novo Nordisk (Advisory Board), Boehringer Ingelheim (Advisory Board). Andrew J. Ahmann, MD, MS—Financial or Business/Organizational Interests: American Diabetes Association (Member/Regional Leadership Council), AACE (Member), Horizon CME (Consultant/Speaker for PriMed), Sanofi (Advisory Board/Research), Novo Nordisk (Consultant/Research Funding), Lilly (Consultant/Advisory Board), Janssen (Consultant/Advisory Board), Dexcom (Research Funding), Medtronic (Research Funding), Lexicon (Research Funding); Significant Financial Interest or Leadership Position: none declared. Tadej Battelino, MD, PhD—Financial or Business/Organizational Interests: Medtronic (Advisory Board/Research Grant to Institution/Speakers Bureau), Novo Nordisk (Advisory Board/Research Grant to Institution/Speakers Bureau), Lilly (Advisory Board/Speakers Bureau), Sanofi (Advisory Board/Speakers Bureau), Bayer (Advisory Board), Abbott (Research Grant to Institution), Sandoz (Research Grant to Institution), Roche (Speakers Bureau); Significant Financial Interest or Leadership Position: DreaMed (Chief Medical Officer/Ownership Interests). Alison Evert, MS, RD, CDE—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: none declared. Irl B. Hirsch, MD—Financial or Business/Organizational Interests: Wolters Kluwer (Editor), Abbott Diabetes Care (Consultant), Roche (Consultant), Intarcia (Consultant); Significant Financial Interest or Leadership Position: none declared. M. Hassan Murad,** MD,MPH—Financial or Business/Organizational Interests: Mayo Clinic Evidence based Practice Center; Significant Financial Interest or Leadership Position: none declared. William E. Winter, MD—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: none declared. Howard Wolpert, MD—Financial or Business/Organizational Interests: Abbott Diabetes Care (Member/Advisory Board), BD (Member/Advisory Board), Bigfoot Biomedical (Member/Advisory Board), Dexcom (Consultant), Glooko (Member/Advisory Board), Insulet (Member/Advisory Board), NovoNordisk (Member/Advisory Board), Zealand (Consultant); Significant Financial Interest or Leadership Position: Abbott Diabetes Care (Member/Advisory Board), BD (Member/Advisory Board), Bigfoot Biomedical (Member/Advisory Board), Dexcom (Consultant), Glooko (Member/Advisory Board), Insulet (Member/Advisory Board), Novo Nordisk (Member/Advisory Board), Zealand (Consultant).

*Financial, business, and organizational disclosures of the Task Force cover the year prior to publication. Disclosures prior to this time period are archived.

**Evidence-based reviews for this guideline were prepared under contract with the Endocrine Society.

Guideline Endorser(s)

American Association for Clinical Chemistry, Inc. - Professional Association

American Association of Diabetes Educators - Medical Specialty Society

European Society of Endocrinology - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Klonoff DC, Buckingham B, Christiansen JS, Montori VM, Tamborlane WV, Vigersky RA, Wolpert H,

Endocrine Society. Continuous glucose monitoring: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011 Oct;96(10):2968-79.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available to subscribers from The Endocrine Society Web site .

Availability of Companion Documents

The following is available:

- Benkhadra K, Alahdab F, Tamhane S, Wang Z, Prokop LJ, Hirsch IB, Raccah D, Riveline J-P, Kordonouri O, Murad MH. Real-time continuous glucose monitoring: a systematic review and individual patient data meta-analysis. Rochester (MN): Knowledge Synthesis Unit, Mayo Clinic; 2016. 23 p.

A clinical practice guidelines mobile app is available for download from The Endocrine Society Web site .

Continuing medical education (CME) activities are also available on The Endocrine Society Web site .

Tables 1 to 3 in the original guideline document provide considerations and resources for education and training in use of the devices.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on June 12, 2012. The information was verified by the guideline developer on June 22, 2012. This summary was updated on May 19, 2017. The updated information was verified by the guideline developer on June 13, 2017.

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